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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/980,772	07/31/2002	Malcolm Roy Brandon	78870/00004	7473

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EXAMINER	
CROUCH, DEBORAH	
ART UNIT	PAPER NUMBER
1632	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/28/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/980,772	BRANDON ET AL.	
	Examiner	Art Unit	
	Deborah Crouch, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23 and 30-43* is/are pending in the application.

4a) Of the above claim(s) *16-19 and 31-33* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15,20-23,30 and 34-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 October 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☒ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on September 15, 2006 has been entered.

Claims 1-23 and 30-43 are pending. Claims 16-19 and 31-33 are withdrawn from consideration as to a nonelected invention. Claims 1-15, 20-23,30 and 34-43 are examined herein.

This case has be docketed to Deborah Crouch, Ph.D., AU 1632.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-15, 20-23, 30 and 34-43 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of preparing a reprogrammed diploid mammalian cell comprising providing a diploid mammalian donor cell or a diploid mammalian donor nucleus and a recipient mammalian oocyte, microinjecting the donor nucleus into the oocyte, removal of the oocyte nucleus, incubation of the reconstructed oocyte, activation of the oocyte to permit develop into embryos, as claimed does not reasonably provide enablement for methods of preparing a reprogrammed diploid mammalian cell from non-mammalian cells or non-mammalian nuclei through the use of a non-mammalian recipient cell, or the production of a mammal, mammalian organs or tissues or animals by the claimed methods. The specification does not enable any person

skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are unpredictable as written as to make a reprogrammed mammalian cell or embryo mammalian donor and recipient cells would need to be used. The use of other species cells would not result in a mammalian cell or embryo. Further, there would necessarily need to be a means to determine the recipient and donor nuclei in the claimed method. The specification only discusses one method of doing such, which is the piezo-impact microinjection system (Wakayama (1998), page 373, col. 2, lines 5-12 and specification, page 30, line 28 to page 31, line 1; and page 33, lines 15-20). The specification provides no other guidance for identifying donor and recipient nuclei. The guidance provided in the specification, is for the microinjection of the donor nucleus followed by immediate removal of the recipient nucleus (specification, page 33, lines 15-27). The now diploid reconstructed oocyte is incubated 3-4 hrs prior to activation and embryo development permitted.

Further, the specification does not enable the production of a mammal, mammalian organs or mammalian tissues by the claimed method. As stated by Pennisi at the time of filing, several scientists working in the area of mammalian cloning point to a lack of general and reproducible success. Robert Wall of the USDA is quoted as stating that despite years of effort, we're in the same bind that we've always been in. A majority of would be clones do not make it to term (Pennisi and Vogel (2000), page 1722, col. 1, parag. 2, lines 9-14). Pennisi and Vogel state that even when an embryo does successfully implant in the womb, pregnancies often end in miscarriages (Pennisi and Vogel (2000), page 1722, col. 1, parag. 3, lines 16-18). Attempts to clone pigs using techniques successful in sheep were not successful; indicating that cross-species application of methodology is unpredictable (Pennisi and Vogel (2000), page 1725, col. 1-2, bridg. parag.). The case with rabbits indicates that

obtaining an embryo by nuclear transfer does not translate into a cloned rabbit. While many cloned rabbit embryos can be made, they abort upon transfer to surrogate mothers, and in 2000, there had not been any successes in cloning rabbits (Pennisi and Vogel (2000), page 1725, col. 2, parag. 3). With primates, two cloned monkeys were produced, but there has been no subsequent success in primate cloning (Pennisi and Vogel (2000), page 1726, col. 2, line 6 to col. 3, line 3). Thus, the specification's demonstration of blastocyst formation is not sufficient to enable the production of an animal or a mammal by the claimed method.

Thus, at the time of filing, the skilled artisan would have needed to engage in an undue amount of experimentation without a predictable degree of success to implement the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-23 and 30-43 are confusing rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 11, 30 and 34 each contain the terms "substantial removal," "substantial destruction" or "substantially removed or destroyed." There is no definition of any of these terms in the specification, and no clear definition in the art. Therefore, the metes and bounds of the claims would not be clear to the reader. It is suggested that applicant delete "substantial" or "substantially" from the claims if a definition cannot be identified.

Claims 1, 30 and 34 are additionally confusing because there is no limitation in the claims that results in a reprogrammed diploid mammalian cell. While a reprogrammed nucleus is a limitation this is not seen as relating back to the preamble. It is suggested that

applicant insert an wherein clause to the effect that the end result of the method is a reprogrammed diploid mammalian cell.

Claims 20-23 are improperly dependent on claim 1. Claim 1 is to a method of preparing a reprogrammed diploid mammalian cell. Claims 20-22 are further comprising the step of generating a cell line, a tissue, an organ or an animal embryo from the reprogrammed cell. Claims 20-23 are not related to a method of reprogramming a cell, but are in fact to methods of using the reprogrammed cell to produce products. Claims 20-22 should be rewritten as independent claims. However, applicant is warned that doing such may result in a restriction by original presentation. Further, claims 20-23 state animal. As such they are broader in scope than claim 1, which indicates in the preamble "mammal."

Claims 37-40 sates a human or a mouse cell according to particular claims. However, the particular claims have been canceled. It is not possible to determine the metes and bounds of claims 37-40 since the limitations set forth in the particular claims are not known.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 37 and 38 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Thomson et al (1998) Science, Vol. 282, pp. 1145-1147.

Thomson teaches a human ES cell (page 1145, col. 2, lines 14-17). Thomson also teaches a mouse fibroblast (page 1145, figure 2A, legend). The human and mouse cells claimed have no patentable distinction over those of Thomson.

[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985).

"The Patent Office bears a lesser burden of proof in making out a case of prima facie obviousness for product-by-process claims because of their peculiar nature" than when a product is claimed in the conventional fashion. In re Fessmann, 489 F.2d 742, 744, 180 USPQ 324, 326 (CCPA 1974). Once the examiner provides a rationale tending to show that the claimed product appears to be the same or similar to that of the prior art, although produced by a different process, the burden shifts to applicant to come forward with evidence establishing an unobvious difference between the claimed product and the prior art product. In re Marosi, 710 F.2d 798, 802, 218 USPQ 289, 292 (Fed. Cir. 1983).

"Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product (*In re Ludtke*). Whether the rejection is based on "inherency" under 35 USC 102, on "prima facie obviousness" under 35 USC 103,

jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. *In re Best, Bolton, and Shaw*, 195 USPQ 430, 433 (CCPA 1977) citing *In re Brown*, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972))."

"When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, the *prima facie* case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product. *In re Best*, 562 F.2d at 1255, 195 USPQ at 433. See also *Titanium Metals Corp. v. Banner*, 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985), *In re Ludtke*, 441 F.2d 660, 169 USPQ 563 (CCPA 1971), *Northam Warren Corp. v. D. F. Newfield Co.*, 7 F. Supp. 773, 22 USPQ 313 (E.D.N.Y. 1934.) See MPEP 2113 and MPEP 2112.01.

Thus Thomson clearly anticipates the claimed invention.

Claims 39 and 40 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Games et al. (1995) Nature, Vol. 373, pp. 523-527.

Games et al teach a transgenic mouse whose genome comprises a nucleic acid sequence encoding an FAD amyloid protein (page 523, co. 2, parag. 2, lines 1-3). The transgenic mouse of the claims has no patentable distinction over that of the Games.

"The Patent Office bears a lesser burden of proof in making out a case of prima facie obviousness for product-by-process claims because of their peculiar nature" than when a product is claimed in the conventional fashion. In re Fessmann, 489 F.2d 742, 744, 180 USPQ 324, 326 (CCPA 1974). Once the examiner provides a rationale tending to show that the claimed product appears to be the same or similar to that of the prior art, although

produced by a different process, the burden shifts to applicant to come forward with evidence establishing an unobvious difference between the claimed product and the prior art product. In re Marosi, 710 F.2d 798, 802, 218 USPQ 289, 292 (Fed. Cir. 1983).

"Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product (*In re Ludtke*). Whether the rejection is based on "inherency" under 35 USC 102, on "prima facie obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. *In re Best, Bolton, and Shaw*, 195 USPQ 430, 433 (CCPA 1977) citing *In re Brown*, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972))."

"When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, the *prima facie* case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product. *In re Best*, 562 F.2d at 1255, 195 USPQ at 433. See also *Titanium Metals Corp. v. Banner*, 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985), *In re Ludtke*, 441 F.2d 660, 169 USPQ 563 (CCPA 1971), *Northam Warren Corp. v. D. F. Newfield Co.*, 7 F. Supp. 773, 22 USPQ 313 (E.D.N.Y. 1934.) See MPEP 2113 and MPEP 2112.01.

Thus Games clearly anticipates the claimed invention.

Claims 1, 2, 4, 7, 11-13, 20, 21, 30, 34, 36 and 41-43 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Clement-Sengewald et al (1990) Reprod. Domestic Animals, Vol. 25, pp. 14-21.

Clement-Sengewald teaches the electrofusion of mouse blastomeres to produce an aneuploid cell (page 16, parag. 1 to page 17, line 26). Blastomeres are diploid cells and meet the limitation of "other pluripotent stem cell," and their nuclei are diploid also. Clement-Sengewald teaches the aneuploid cells were incubated for 1 hr 15 min to 1 hr 45 min prior to removal of the cell nucleus by micromanipulation (page 17, lines 7-11). Either cell nucleus is considered the recipient. The incubation time is suitable for the nucleus to be reprogrammed as evidenced by the production mouse embryos and the birth of live-born mice (page 20, parag. 2; page 21, lines 1-2; and 20, Table 3). The blastomeres inherently form an animal embryo containing pluripotent embryonic cells. Thus Clement-Sengewald clearly anticipates the claimed invention.

Claims 1 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Clement-Sengewald et al (1990) Reprod. Domestic Animals, Vol. 25, pp. 14-21 in view of Wakayama et al (1998) Nature 394, pp. 369-374.

Clement-Sengewald teaches the electrofusion of mouse blastomeres to produce an aneuploid cell (page 16, parag. 1 to page 17, line 26). Blastomeres are diploid cells and their nuclei are diploid also. Clement-Sengewald teaches the aneuploid cells were incubated for 1 hr 15 min to 1 hr 45 min prior to removal of the cell nucleus by micromanipulation (page 17, lines 7-11). Either cell nucleus is considered the recipient. The incubation time is suitable for the nucleus to be reprogrammed as evidenced by the production mouse embryos and the birth of live-born mice (page 20, parag. 2; page 21, lines 1-2; and 20, Table 3).

Wakayama teaches the production of mice by injection of a cumulus cell nucleus into an enucleated MII arrested oocyte by piezo-impact pipette drive unit, where the oocyte and nucleus are fused by piezo, where activation is simultaneous with injection, 1-3 hours after injection or 3-6 hours after injection, embryos transferred to a surrogate female mouse and

developed to term (page 369, 2, 4-9; page 370, table 3; and page 373, col. 1, lines 9-16 and col. 2, lines 15-16). The oocyte-nucleus complex was activated by incubation in media containing Sr+2 and cytochalasin B (page 369, col. 2, lines 4-9). Wakayama offers motivation for piezo-impact microinjection in stating a high rate of embryonic development because donor cell and recipient oocyte manipulations were quicker and more efficient (page 373, col.1, lines 11-19).

Thus, at the time of the instant invention, it would have been obvious to the ordinary artisan to prepare reprogrammed diploid mammalian cells or embryos by first producing an aneuploid cell and removing the recipient nucleus as taught by Clement-Sengewald modified by using piezo-impact microinjection as taught by Wakayama to improve efficiency.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah Crouch, Ph.D. whose telephone number is 571-272-0727. The examiner can normally be reached on M-Fri, 6:00 AM to 3:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Deborah Crouch

Deborah Crouch, Ph.D.
Primary Examiner
Art Unit 1632

February 20, 2007